(FILE 'MEDLINE, CANCERLIT, EMBASE, BIOTECHDS' ENTERED AT 16:46:19 ON 19 DEC 2003)

DEL HIS

L1	12595	S	CYCLODEXTRIN
L2	32887	S	LIPOSOME OR AMPHIPHILE OR CATIONIC LIPID
L3	98289	S	CONJUGATED OR COMPLEXED OR ELECTROSTATICALLY OR IONICALLY OR
L4	156	S	L2 AND L1
L5	134	S	L4 NOT ENCAPSULA?
L6	9	S	L5 AND L3
L7	9	DUP REM	L6 (0 DUPLICATES REMOVED)
L8	3243831	S	DNA OR NUCLEIC OR POLY? OR PLASMID
L9	45	S	L8 AND L5
L10	42	DUP REM	L9 (3 DUPLICATES REMOVED)

L7 ANSWER 7 OF 9 EMBASE COPYRIGHT 2003 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

AN 1999142466 EMBASE

TI Hydrocortisone/**cyclodextrin** complex: Complexation methods and complex incorporation in liposomes.

AU Becirevic-Lacan M.; Skalko N.

CS M. Becirevic-Lacan, Department of Pharmaceutics, Faculty of Pharmacy and Biochemistry, University of Zagreb, A. Kovacica 1, 10000 Zagreb, Croatia

SO S.T.P. Pharma Sciences, (1997) 7/5 (343-347).
Refs: 13
ISSN: 1157-1489 CODEN: STSSE5

CY France

DT Journal; Article

FS 037 Drug Literature Index
039 Pharmacy

LA English

SL English; French

AB Hydrocortisone acetate was **complexed** with .gamma.-**cyclodextrin** to form a hydrocortisone/**cyclodextrin** inclusion complex. Two complexation methods were applied, i.e. the coprecipitation and spray-drying methods. Drug alone, hydrocortisone/**cyclodextrin** complex I and hydrocortisone/**cyclodextrin** complex II were incorporated into liposomes destined for topical application. The highest achieved entrapment of the drug was equal for liposomes containing hydrocortisone or hydrocortisone/**cyclodextrin** complex II. The complexation method (spray-drying) and **liposome** preparation method (dilution of proliposome mixture) are simple and exhibit great potential for industrial production.

L10 ANSWER 33 OF 42 BIOTECHDS COPYRIGHT 2003 THOMSON DERWENT/ISI on STN
AN 1998-10876 BIOTECHDS
TI Use of **polynucleotide** compositions;
for intra-pericardial delivery for treatment or prevention of cardiovascular indications e.g. cardiomyopathy, occlusions or inflammation
AU Hung D T
PA Chiron
LO Emeryville, CA, USA.
PI WO 9716169 9 May 1997
AI WO 1996-US17311 30 Oct 1996
PRAI US 1996-726346 28 Oct 1996; US 1995-7158 1 Nov 1995
DT Patent
LA English
OS WPI: 1997-271858 [24]
AB A method of treatment or prevention of a wide range of cardiovascular indications is claimed and comprises administering a **polynucleotide** (a **plasmid** or a viral vector e.g. an adeno virus) associated with a **liposome**, **cyclodextrin liposome**, heterovesicular **liposome**, synthetic membrane vesicle, gel, etc., and a therapeutic agent composition intra-pericardially to a patient. The **polynucleotide** may encode basic fibroblast growth factor, tumor necrosis factor-alpha, heparin, antibody, hepatocyte growth factor, proliferin, insulin-like growth factor, etc., transfected using a ribozyme, antisense oligonucleotide, antibody, etc. Also claimed is a kit for such a delivery. The method can be used for treating a wide range of cardiovascular disorders including coronary artery occlusion resulting from or associated with lipid/cholesterol deposition, thrombosis, angina, and also metabolic disease e.g. glycogen storage disease, neuromuscular disease, trauma, inflammatory conditions, connective tissue diseases, bacterium, virus, fungus or parasite infection. A higher transduction efficiency is afforded by pericardial administration. (70pp)

L10 ANSWER 12 OF 42 EMBASE COPYRIGHT 2003 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

AN 2003284904 EMBASE

TI [Enhanced liposomal transfection through the application of sexsteroids in gynecological cancer cells].
DIE SEXUALSTEROID-VERMITTELTE VERSTARKUNG LIPOSOMALER TRANSFEKTION GYNAKOLOGISCHER KREBSZELLEN: EIN NEUER ANSATZ FUR EIN SELEKTIVES TARGETING IN DER GENTHERAPIE?.

AU Koster F.; Finas D.; Saupp A.; Schulz C.; Diedrich K.; Hauser C.; Felberbaum R.

CS Dr. R. Felberbaum, Klin. Frauenheilkunde/Geburtshilfe, Universitat zu Lubeck, Ratzeburger Allee 160, 23538 Lubeck, Germany.
RFelberbau@netscape.net

SO Zentralblatt fur Gynakologie, (1 Jan 2003) 125/1 (1-5).
Refs: 16
ISSN: 0044-4197 CODEN: ZEGYAX

CY Germany

DT Journal; General Review

FS 003 Endocrinology
016 Cancer
029 Clinical Biochemistry

LA German

SL English; German

AB Objective: Liposomal transfection in gene therapeutic application against gynecological malignoma does not reach satisfying efficacy. A desirable goal would be the specific intensification of transfection in these kind of cells. Steroids have successfully been used in other systems to increase liposomal transfection and hopefully there might be a specific impact of sexual steroids in cells from high sex steroid receptor expressing malignoma, like some mamma- and endometrium cancer. Material and Methods: The mamma carcinoma cell line T-47D was transfected with the transfection agent DOTAP and **cyclodextrin** solubilized steroids and cholesterol were co-applied. The efficiency of transfection was followed by luciferase activity resulting from the transfected reporter gene. Results: Like cholesterol, which is already established as transfection co-agent, also the steroids progesterone, estrogen, testosterone and hydrocortisone provoked a clear increase in transfection efficiency shown in a dose dependent manner. Conclusions: These results indicate the usefulness of steroids as additives for liposomal transfection procedures in gene therapeutic application. As sexual steroid receptors migrate into the nucleus of a cell after binding its specific ligand a targeted enhancement of transfection is supposable in malignoma overexpressing steroid receptors. There is evidence that **plasmid DNA** can be co-transported with nuclear proteins into the nucleus.

forming a functional oligomer with 228 kDa.

L10 ANSWER 3 OF 42 MEDLINE on STN DUPLICATE 1
AN 2003476423 IN-PROCESS
DN 22915974 PubMed ID: 14555526
TI Nonviral cytokine gene therapy on an orthotopic bladder cancer model.
AU Wu Qinghui; Mahendran Ratha; Esuvaranathan Kesavan
CS Department of Surgery, National University of Singapore, Singapore 119074.
SO CLINICAL CANCER RESEARCH, (2003 Oct 1) 9 (12) 4522-8.
Journal code: 9502500. ISSN: 1078-0432.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS IN-PROCESS; NONINDEXED; Priority Journals
ED Entered STN: 20031014
Last Updated on STN: 20031021
AB PURPOSE: The purpose is to assess cytokine gene transfection in tumor cells and its therapeutic efficacy in an orthotopic mouse bladder cancer model after **liposome**-mediated gene transfer. EXPERIMENTAL DESIGN: A total of 1 x 10(5) MB49 cells was instilled into the bladder of C57BL/6 mice after electrocautery to establish the tumor model. The plasmids were constructed by inserting the coding sequences for murine IFN-alpha1 and granulocyte macrophage colony-stimulating factor into a **plasmid** vector pBudCE4.1. Transient transfection was performed using a **cationic lipid** N-[1-(2,3-dioleoyloxyl)propyl]-N,N,N-trimethylammoniummethyl sulfate and methyl-beta-**cyclodextrin**-solubilized cholesterol. The in vitro expression of cytokines was checked by ELISA. The expression of the transgene in situ was confirmed by immunohistochemistry and 5-bromo-4-chloro-3-indolyl-beta-D-galactopyranoside staining. Mice bearing orthotopic tumors were treated with **plasmid DNA/liposome** complex by intravesical instillation twice a week for 3 weeks. RESULTS: Superficial bladder tumors were established by intravesical instillation of MB49 into cauterized bladders. The expression level of cytokines in transfected cell lines was increased significantly. In situ gene transfer to bladder tumors was accomplished via intravesical instillation of **plasmid DNA**/N-[1-(2,3-dioleoyloxyl)propyl]-N,N,N-trimethylammoniummethyl sulfate/methyl-beta-**cyclodextrin**-solubilized cholesterol after a single 2 h in situ transfection. The tumor incidence in the treatment groups was dramatically decreased from 76.9% in the control group to 15.4-30.8% in the treatment groups. CONCLUSIONS: We demonstrated in the orthotopic mouse bladder cancer model that successful inhibition of tumor cell growth could be obtained with cytokine gene therapy. The results suggest that our **liposome** transfection system appears to be a promising method for gene therapy of bladder cancer in vivo.

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L16	l12 with l14	932	L16
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L14	amphiphile or lipid or liposome	110265	L14
L13	electrost$ or non-covalen$ or ionic or complexed or conjuga$	650083	L13
L12	cyclodextrin	18492	L12
L11	5691387.pn.	2	L11
L10	6359014.pn.	2	L10
L9	5674911.pn.	2	L9
L8	l6 same l5	15	L8
L7	l6 same l5L6	0	L7
L6	fusogenic	1908	L6
L5	l4 with l3	217	L5
L4	liposome	45468	L4
L3	L2 or l1	2135	L3
L2	Sendai virus	2121	L2

First Hit

L17: Entry 10 of 25 File: PGPB Feb 6, 2003

DOCUMENT-IDENTIFIER: US 20030026781 A1
TITLE: Compositions and methods for regulating endogenous inhibitor of ATP synthase, including treatment for diabetes

Detail Description Paragraph:
[0353] The nucleic acid molecules can be complexed with cationic lipids, packaged within liposomes, incorporated into hydrogels, cyclodextrins, biodegradable nanocapsules, or bioadhesive microspheres. The pharmaceutical composition may include carriers, thickeners, diluents, buffers, preservatives, surface active agents, and the like in addition to oligonucleotides. Pharmaceutical compositions can also include one or more active ingredients such as antimicrobial agents, antiinflammatory agents, anesthetics, and the like in addition to oligonucleotides. If administration is by injection or infusion, the nucleic acid molecules can be delivered directly or in the aforementioned compositions in sterile solution, which may also contain buffers, diluents, and other suitable additives. Formulations for topical administration may include ointments, lotions, creams, gels, drops, suppositories, sprays, liquids, and powders. Conventional pharmaceutical carriers, aqueous, powder or oily bases, thickeners and the like can be necessary or desirable.

Detail Description Paragraph:
[0367] Gene therapy constructs that consist of nucleic acid molecules not incorporated into vectors such as viruses may be delivered as free nucleic acids, or may be delivered covalently or noncovalently conjugated or bound to other molecules, such as, but not limited to, molecules that enhance their transport across the blood-brain barrier or that may facilitate their delivery to the target tissue or tissues. Other DNA sequences, such as adenovirus VA genes can be included in the administration medium and be co-transfected with the gene of interest. The presence of genes coding for the adenovirus VA gene product may significantly enhance the translation of mRNA transcribed from the plasmid. Gene therapy constructs that are packaged in viruses may have proteins or other molecules or compounds, such as, but not limited to lipids, proteins, or polymers incorporated into or associated with the virus to enhance delivery into cells. The gene therapy constructs, whether naked DNA or packaged vector constructs, may be complexed with cationic lipids, packaged within liposomes, incorporated into hydrogels, cyclodextrins, biodegradable nanocapsules, or bioadhesive microspheres. The pharmaceutical composition may include carriers, thickeners, diluents, buffers, preservatives, surface active agents, and the like in addition to oligonucleotides. Pharmaceutical compositions may also include one or more active ingredients such as antimicrobial agents, antiinflammatory agents, anesthetics, and the like in addition to oligonucleotides. If administration is by injection or infusion, the gene therapy constructs may be delivered directly or in the aforementioned compositions in sterile solution, which may also contain buffers, diluents, and other suitable additives. Formulations for topical administration may include ointments, lotions, creams, gels, drops, suppositories, sprays, liquids, and powders. Conventional pharmaceutical carriers, aqueous, powder or oily bases, thickeners and the like may be necessary or desirable.

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L17: Entry 11 of 25 File: PGPB Sep 26, 2002

DOCUMENT-IDENTIFIER: US 20020137762 A1
TITLE: Delivery systems and methods for noscapine and noscapine derivatives, useful as anticancer agents

CLAIMS:

12. The delivery system of claim 11, wherein the compound is complexed with cyclodextrins and encapsulated by liposomes.

L17: Entry 19 of 25 File: USPT Jun 2, 1998

DOCUMENT-IDENTIFIER: US 5759573 A
**** See image for Certificate of Correction ****
TITLE: Cyclodextrin liposomes encapsulating pharmacologic compounds and methods for their use

Detailed Description Text (2):
The present invention is directed to forming inclusion complexes of water-soluble compounds, such as methotrexate, with cyclodextrins, preferably .beta.-cyclodextrin, and to encapsulating the inclusion complex into liposomes for controlled release. For use in the practice of this invention the cyclodextrin preferably forms an inclusion complex with the water soluble compound wherein the apolar cavity of the cyclodextrin is occupied by or sequesters the compound sufficiently to slow the rate of release from the liposome composition. The rim or the periphery of the inclusion complex is hydrophilic with the result that the inclusion complex forms a solution in aqueous media. The cyclodextrin-complexed water soluble substance can then be encapsulated into liposomes.

CLAIMS:

1. A liposome comprising

water,

a biologically active, eater soluble compound encapsulated within the liposome, and

a cyclodextrin in a concentration of from about 10 mg/ml to about 400 mg/ml complexed with the compound within the liposome,

wherein the biologically active compound is released from the liopsome into an aqueous solution at about 37.degree. C. at a slower rate than from a cyclodextrin-free liopsome, and without substantial compromise to the therapeutic index of the biologically active compound.

18. A method of increasing the half-life of a water soluble biologically active compound in an animal in need thereof comprising administering to the animal a liposome encapsulating the compound, wherein said liposome further encapsulates water, and a cyclodextrin in a concentration from about 10 mg/ml to about 400 mg/ml complexed with said compound; whereby the half-life of the compound is substantially increased.

33. A method of treating a pathophysiological state in an individual in need thereof comprising administering a liposome to the individual, said liposome comprising a therapeutically effective amount of a water soluble, biologically active compound complexed with a cyclodextrin, wherein the concentration of the cyclodextrin is from about 10 mg/ml to about 400 mg/ml, and the biologically active substance and the cyclodextrin are encapsulated within the liposome; whereby the half-life of the compound in the individual is substantially increased.

L17: Entry 21 of 25 File: USPT Dec 6, 1994

DOCUMENT-IDENTIFIER: US 5371209 A
**** See image for Certificate of Correction ****
TITLE: Process for separating cyclodextrin from a complex

Brief Summary Text (20):
In some cases, the solution of complexed cyclodextrin and lipid has food particles which are proteins. This is especially true for complexes obtained from the decholesterizing of egg yolks. These egg proteins have been found to make the separation of the decomplexed cyclodextrin from the residual protein very difficult. Specifically, it has been found that in certain instances these proteins form gels which substantially hinder the recovery of the cyclodextrin from solution or the recycling of a substantially pure cyclodextrin-salt solution. Such proteins are often present with the solution of complexed cyclodextrin and guest not only from the decholesterizing of eggs but also from the decholesterizing of milk products, especially milk itself.

L17: Entry 23 of 25 File: USPT Jan 19, 1993

DOCUMENT-IDENTIFIER: US 5180716 A
**** See image for Certificate of Correction ****
TITLE: Cyclodextrin complexes for neuraxial administration of drugs

Detailed Description Text (11):
The freedom with which a complexed drug may exit the environment of the cyclodextrin cavity is a function of the size of the drug molecule, its shape, and its lipid solubility. Lipophilic drug molecules bind with greater affinity to the hydrophobic interior of the cyclodextrin. If the lipid solubility of the drug is too high, the drug may not dissociate at all, even when the complex approaches a lipid membrane; thus, some drugs would be rendered inactive since they would not reach specific receptors in tissue in an active form. In its simplest form, the interaction between a drug and a cyclodextrin resembles that of a competitive ligand, and as such obeys the law of mass action with affinity proportional to the lipid solubility and other physicochemical properties of the drug. Pitha, J.: Neurotransmissions Research Biochemicals, Inc., Massachusetts 5 (1989).